REMARKS

Reconsideration of the Examiner's rejection of the present application is requested respectfully in view of the above amendments and the following remarks.

STATUS OF THE CLAIMS

Claims 1-5 and 7 are pending, and claim 6 was previously canceled. Claim 1 has been amended. No other claims have been amended, added or deleted.

SUMMARY OF OFFICE ACTION

Claims 1-5 and 7 stand rejected under 35 U.S.C. §103(a) as being obvious over Nestor et al. (EP 0472 220) ("Nestor") in view of Henke et al (US 5,648,333) ("Henke").

Claims 1-5 also stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 27-28 and 30 of Henke, in view of Nestor.

THE REJECTION UNDER 35 U.S.C. §103(a)

The primary reference in this rejection is Nestor et al (EP 0472 220). As a preliminary point, Nestor et al (EP 0472 220) is the equivalent of Nestor et al (AU 638 350), which is cited on page 1 of the present specification. For clarity, unless indicated otherwise, all references to "Nestor" will be directed to the above-cited EP document.

In the present action, the Examiner has cited Nestor as teaching that "bradykinin promotes matrix degradation", with reference to page 2, lines 30-36 of the EP document. In the cited passage, Nestor in turn cites a Lerner et al. article from *Arthritis and Rheumatism* ("Lerner"), which was cited on page 1 of the present specification in connection with the citation of the Nestor AU reference. A copy of this article is provided herewith in a separate IDS. Although Nestor mentions "matrix degradation", it is clear from a full reading of the Lerner article that the reference is to bone matrix degradation, not the degradation of the cartilage components of a joint. In particular, line 5 the Abstract of the Lerner article speaks of "bone mineral mobilization and matrix degradation", but later the Abstract states "Bradykinin ... did not affect the degradation of cartilage proteoglycans...". For this reason, it is stated at page 1, lines 35-37 of the present specification that Lerner teaches that "...bradykinin may actually

enhance bone resorption, but does not stimulate degradation of the cartilaginous matrix itself." Clearly, there is a distinction between matrix degradation of bone, and matrix degradation of the cartilaginous materials in joints.

To emphasize this distinction, present claim 1 has been amended to claim a "method for treating a degenerative joint disease which includes **cartilaginous** matrix degradation...selected from the group consisting of osteoarthrosis, spondyloses and cartilage atrophy". As such, the Lerner reference, and hence the Nestor reference, clearly teach away from the present invention. There is no teaching in Nestor or Lerner that bradykinin promotes degradation of the cartilaginous matrix of joints, and therefore no teaching that a bradykinin antagonist could be used in the treatment of joint diseases such as osteoarthrosis, spondyloses and cartilage atrophy. For these reasons, the Examiner is respectfully requested to reconsider the use of the Nestor reference as the primary reference in the present rejection.

In the present rejection, the secondary reference is Henke et al, which is cited as teaching the compounds of the present invention and there use for treating "all pathological states which are mediated, caused or supported by bradykinin...". However, as discussed above, the Nestor reference does not teach that the presently claimed degenerative joint diseases are mediated, caused or supported by bradykinin. Instead, the Lerner article clearly indicates in the detailed discussion at pages 535-536 thereof, that "... the addition of bradykinin ... did not affect the release of ^{35}S-sulfate from articular cartilage...". Yet the article goes into great detail on the resorption of bone matrix from selected mouse bones. Therefore, a review of this article shows a distinction in the action of bradykinin on a cartilaginous matrix as compared to a bone matrix. With this reference in mind, it is clear that although Henke teaches that bradykinin inhibition may be useful for treating the painful symptoms of osteoarthritis or rheumatoid arthritis, there is no teaching that bradykinin inhibitors would be useful for treating bone matrix degradation, which is the underlying cause of the degenerative joint diseases to which the present invention is directed.

Therefore, for the reasons discussed above, it is submitted that there is no teaching in Nestor, alone or in combination with Henke, of the use of the bradykinin inhibitor compounds of present claim 1 to treat degenerative bone diseases by inhibiting cartilaginous matrix degradation. The Examiner is respectfully requested to reconsider and withdraw the rejection of the present claims over these references.

THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION

Claims 1-5 and 7 also stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 27-28 and 30 of Henke et al, in view of Nestor. Applicants respectfully traverse this rejection.

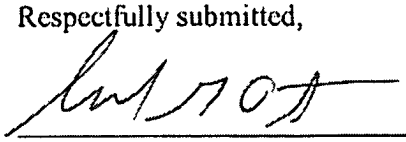
The cited claims 27-28 and 30 of Henke et al are directed to compositions and methods for treating a variety of specified conditions including arthritis. There is nothing in these claims about the treatment of degenerative joint diseases such as osteoarthrosis, spondyloses or cartilage atrophy, and certainly no discussion of treating them by inhibiting cartilaginous matrix degradation. Although a wide variety of pathological states are included in these claims, and although degenerative joint diseases have been known for many years, yet there is no teaching or claim in Henke et al directed to the treatment of such diseases. The cited claims include a variety of inflammatory diseases, and other diseases which may cause a great deal of pain. However, there is no indication in these claims that the bradykinin inhibitors may be used for the treatment of cartilage matrix degradation associated with degenerative joint diseases.

In this rejection, Nestor is cited as a secondary reference to show that such joint diseases are induced or mediated by bradykinin. However, as discussed above, applicants submit that there is no such teaching in Nestor. Therefore, for the reasons discussed here and in the previous part of this response, the Examiner is respectfully requested to reconsider and withdraw this obviousness-type double patenting rejection of the present claims.

For all of the above reasons, it is submitted that all of the claims in the present application are now in condition for allowance, and action to that effect is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees or credit any overpayment resulting from this Amendment to Deposit Account 18-1982.

Respectfully submitted,



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